THE AMERICAN JOURNAL OF Clinical Nutrition

NOVEMBER–DECEMBER 1957 VOLUME 5, NUMBER 6

The Role of Protein in Diets for Weight Reduction

By VINCENT P. DOLE, M.D.

IN PRESCRIBING a diet for the reduction of obese patients one can choose between a low-calorie diet with an exceptionally high proportion of protein, or a diet with normal proportions of the various nutrients, but limited in total quantity. A century of clinical tradition[1] favors the first alternative. However, it might be proper at this time to re-examine the tradition.

Recent biochemical studies have revealed an unexpected metabolic activity of lipids in the fat stores; adipose tissue has been shown to have a significant complement of enzymes and synthetic capacities; various kinds of experimental obesities have been discovered and studied; new kinds of diets have been tested in metabolic experiments; the bulk composition of the human body has been estimated by indirect methods; the effects of starvation in wartime have been scrutinized in unprecedented detail. It would be surprising indeed if all this new evidence did not require some enlargement of our opinions.

Basic to much of the older thought on weight control was the assumption that the body could be divided into living protein material and dead storage matter.[2,3] It seemed evident that obesity, defined as an excess of inert fat added to an otherwise normal body,[1,4] should be treated with a diet that would eliminate the fat and preserve the "living tissue." Today, it is clear that the original conception of obesity was too simple. Fat tissue is neither inert, nor is it the only tissue that varies when weight is changed. It is not even certain that any reduction diet can transform an obese person into one with normal body composition and normal functional balance between the different tissues.

As a practical matter the main issues can be summed up in three questions: (1) Does a loss of nitrogen always cause damage to vital structures? (2) Is it desirable for an obese person to lose any nitrogen during weight reduction? (3) Does an exceptionally high proportion of protein in a low-calorie diet make the weight loss easier or faster? These will be taken up in order.

LOSS OF NITROGEN

Historically, numerous studies of nitrogen balance during underfeeding of both protein and calories were conducted in efforts to correlate metabolic rate and level of protein metabolism.[5] No damage to health was reported as incident to the nitrogen loss in the experiments. Benedict[6] and more recently Keys,[7] in comprehensive experiments conducted under close medical supervision, observed average total nitrogen losses of 175 and 430 g, respectively, roughly 24 and 27 g nitrogen/kg weight loss. Neither of these careful observers reported any dangerous symptoms associated with the nitrogen loss, or found any evidence in their follow-up studies suggesting a damage of vital structures.

From the Hospital of The Rockefeller Institute, New York, New York.

On the other hand, unbalanced high-calorie, low-protein, and vitamin-deficient diets can injure the liver, especially if they are fed to young, rapidly growing animals.[8–11] The abnormal mixtures used in these experiments have little counterpart in human nutrition, except for the high-carbohydrate, low-protein diets that cause the kwashiorkor syndrome in infants,[12] and the diets of some alcoholics who combine an excess of calories with a deficiency of protein and vitamins. These results are important in that they emphasize the need for a balanced proportion of nutrients in any diet, but certainly there is room to doubt whether experiments with harmful high-calorie diets have any relevance to the problem of weight reduction. All of the experimental studies agree in finding a high-calorie level essential for production of liver damage.[10] A careful search of the literature has failed to reveal *any* experiment in which liver disease or other nutritional lesion has followed simple restriction in the amount of a balanced diet (i.e., a food mixture with all nutrients in the relative proportions of a normal maintenance diet, fed in limited total quantity).

When both calories and protein were restricted in wartime diets, liver disease did not occur. Sherlock[13] employing biopsy and multiple liver function tests in a study of twenty-one malnourished German civilians, concluded that the apparent deficiency of lipotropic factors had failed to cause hepatic necrosis, cirrhosis or fatty change. Helwig-Larsen *et al.*[14] in an extensive study of starvation in German concentration camps, and of postwar rehabilitation, did not encounter acute liver failure or chronic liver damage. Epidemics of infectious hepatitis occurred in some camps, but appeared to run a normal course without unusual complications or subsequent cirrhosis. Extreme caloric deficit and wastage of muscular protein during imprisonment caused no structural damage that could be detected by ordinary clinical examination of 1,479 adult subjects after rehabilitation. Various studies of medical conditions in Japanese prison camps during the recent war showed no significant incidence of liver disease, although a considerable damage might have been expected from the unbalanced diets and the associated vitamin deficiencies.[15,16] Taking the prison camp medical literature as a whole, it is clear that the normal or the obese adult can adapt to caloric restriction and extreme loss of body nitrogen without suffering irreversible damage of vital tissues.

NITROGEN LOSS IN OBESITY

The desirability of any nitrogen loss is of course a separate question. The obese person has an obvious excess of carbon and hydrogen in his body. Does he also have an abnormal quantity of nitrogen? Can we, by diet, restore him to normal composition, and not merely to a statistically normal weight with abnormal proportions of lean and fatty masses? On these points the evidence is scanty and mainly indirect.

Simple overnutrition, produced by eating excess food, causes a much greater retention of nitrogen than can be attributed to the formation of adipose tissue with a nitrogen content of about 1.5 g/kg.[17] In experiments reported in the older literature, reviewed by von Noorden[18] and Grafe,[19] it was consistently found that overfeeding of calories produced massive retentions of nitrogen. The nitrogen to weight-gain ratios, calculated from the data in these reports, ranged from 16 to 28 g/kg. Two recent studies of overfeeding, one reporting nitrogen balance during two weeks of dietary excess,[20] and the other a densitometric measurement of body composition after six months of gain,[21] showed average values of the nitrogen to weight-gain ratio of about 18 and 7 g/kg, respectively. Adult animals, when fattened by liberal feeding and restriction of activity, retain nitrogen.[22] A popular theory attributes clinical obesity to simple overeating.[23] Since all available evidence indicates that the nitrogen retention during caloric overfeeding exceeds the amount in adipose tissue, no doubt advocates of this theory would agree that some nitrogen should be eliminated in treatment.

Keys[24] has provided more direct evidence that cellular material as well as fat is increased in human obesity. Estimations of "obesity tissue"—the excess matter found in the obese subject as compared with the normal, when body composition is determined by density or water content—showed 10 to 30 per cent cellu-

lar material, equivalent to 3 to 10 g of nitrogen/kg of excess weight. If the goal of a reduction diet is the removal of obesity tissue, these figures indicate that at least 3 g of nitrogen/kg of weight loss should be eliminated.

In mice made obese by injection of gold thioglucose, the total nitrogen of the carcass has been reported as both normal[25] and increased.[26] Total nitrogen, however, measures essentially the muscle mass, and this in turn depends on the activity of the animal. Of more specific interest is the finding of a 50 per cent increase in liver mass in three different kinds of experimental obesity—gold thioglucose, genetic, hypothalamic.[25] Apparently there is a true hypertrophy of cellular material in the liver of the gold thioglucose-treated mice, since the dry, defatted weight of the organ was found to be increased.[27] The liver weight of obese human subjects apparently has not been studied in any systematic way, but the frequent abnormalities of liver function,[28] and the high correlation between excess body weight and deaths from hepatic or biliary disease[29] suggest that the liver may be involved in clinical obesity.

Studies of carcass composition after reduction of genetically obese mice[30] and after maintenance of hyperphagic rats in a reduced state by pair feeding with normals,[31] showed a decrease of total nitrogen and liver weight, and a relative excess of body fat. Evidently, the abnormal relation between cellular material and quantity of fat in these animals was determined by a metabolic disease rather than by the composition of their diet, since the obese mice and controls ate identical food mixtures. There appear to be no comparable studies of obese human subjects.

The obese patient tends to conserve nitrogen when the caloric intake is restricted.[32,33] The reason for this is obscure. It is difficult to see how a larger caloric surplus spares the nitrogen stores of obese people more efficiently than a normal amount of stored energy[34] protects people of average weight. Indeed, with respect to nitrogen balance the obese patient behaves more like an undernourished than an overnourished person.

Evaluating the limited evidence available, it appears that the obese patient combines a probable excess of nitrogen in his body with an abnormal tendency to conserve it during caloric starvation. The best treatment of obesity presumably would eliminate excess cellular material as well as excess fat, but only a tentative conclusion is possible at the present time. Evidently, much more work is needed to define body composition in the obese and reduced states, and to determine the sites of nitrogen accumulation and loss.

DIET THERAPY

The acceptability of a reduction diet often is interpreted in terms of a satiety value, which is a subjective term with variable meanings. As measured by actual consumption in unrestricted diets, protein foods obviously have a taste appeal, since the amount of meat and dairy products increases significantly when purchasing power rises above a marginal level.[35] However, the increase of protein is but part of a general caloric expansion; an analysis of the statistics shows a fairly constant proportion of protein calories over the whole range of dietary groups. Recent studies of food consumption in 32 countries[36] and in urban families of the United States[37] show that protein calories accounted for a strikingly constant fraction, 10 to 13 per cent, of total energy intake, despite wide differences in the kind of food eaten and a twofold range of calorie level.[38]

On starting a reduction diet, many patients find it hard to accept a restriction of protein foods;[39] but initial reactions are not necessarily a measure of long-term acceptability. With any diet the decisive test of its practical value is usage during a long course of steady weight loss. On this basis both high- and low-protein diets have demonstrated some value.

Strang, McClugage, and Evans, acting on the theory that a high proportion of protein would sustain the metabolic rate,[40] induced their patients to take about 60 g of protein per day in a 360 cal diet, thus furnishing about two-thirds of the calories as protein. As Evans pointed out,[41] "the menus make no concessions to gustatory sensualism," but in his clinic this diet was remarkably successful. Possibly it was near the upper limit of a practical high-protein diet. Rony,[42] discussing a diet with an

even greater proportion of protein, stated that "most obese patients refuse to follow it for any length of time." Mason,[43] on the other hand, reported satisfactory results with a reduction diet providing only 23 to 33 g protein per day. Our experience agrees with his. Patients treated with low-protein diets,[44] or with milk formulae providing 10 per cent of calories as protein,[45] have been willing to continue treatment for periods of several months. Some patients claimed that it was easier to follow one of these diets than the more traditional schemes, but a new plan always evokes some enthusiasm. The important point is that patients will accept a low-calorie diet containing only a normal proportion of protein, and stay with it long enough to lose a substantial amount of weight.

The theory that high-protein diets stimulate metabolic rate,[37] and thus accelerate weight loss, is not supported by actual tests. High-protein diets have been found to cause no faster losses of weight than isocaloric low-protein diets.[46,47] More specialized aspects of protein metabolism, stimulation of gastric juice[48] or rise of skin temperature in relation to dietary protein and calories,[49] have a physiologic interest but no obvious relevance to the practical design of a reduction diet.

As a proof of satiety in the objective sense of the word, protein added to an ample diet should reduce the total calorie intake when fat and carbohydrate calories remain freely available. This effect has been demonstrated in experimental animals only at very high levels of dietary protein; variations within the moderate range appear to have little or no influence on food intake.[50] Evans' diet,[41] containing such an abnormally high percentage of protein, may have depressed appetite in this way; other reduction diets with more moderate proportions of protein probably are not within the range for a significant effect on appetite. On the other hand, the results of one clinical study suggest that caloric appetite can be limited by reduction of protein intake. When dietary protein was limited to about 35 g/day, and other foods were available in surplus, the patients responded with a voluntary reduction of non-protein calories,[44] similar to the proportional limitation of calories and protein seen in diets of the poorer nations.[36] This is not to say that the subjects enjoyed the restriction of protein. All that was observed, or claimed by the authors, is that, subject to the restriction of protein, the patients chose to eat less non-protein calories. Apparently the obese patients, and the normal weight people in poor countries, elect a low-calorie diet in preference to one with an "abnormal" protein-calorie proportion.

So long as the metabolic causes of obesity remain unknown, the choice of a reduction diet must depend on practical experience rather than theory. The variety of temporarily successful treatments described during the past century make it obvious that the enthusiasm and gentle persistence of a physician,[51] the promotion of physical activity,[52] and control of general living habits count for much more in practical weight reduction than any chemical feature of the reduction diet.

SUMMARY

The published evidence indicates that obese patients can safely lose nitrogen during weight reduction. It suggests that some loss of nitrogen may be a proper part of reduction, since the obese subject probably has more than a normal amount of nitrogen in his body. Although in principle it is clear that the aim of a reduction diet should be a normal body composition, as well as a normal weight, there are no reported studies that relate the proportions of different reduction diets to changes in body composition. As an empirical measure for causing weight loss, a high-protein diet has no proven advantage over simple quantitative limitation of a diet containing a normal proportion of protein.

REFERENCES

1. HARVEY, J.: *Corpulence, Its Diminution and Cure, without Injury to Health*, ed. 4, John Smith, London, 1864.
2. LUSK, G.: Citation of VON VOIT, C. 1881, in *The Elements of the Science of Nutrition*, ed. 3, Saunders, Philadelphia, 1917, p. 74.
3. MILROY, A. J.: Citation of PFLUGER, 1893, in *Metabolism and General Medicine* (C. VON NOORDEN), Vol. 1, W. T. Keener, Chicago, 1907, p. 287.

4. STRANG, J. M., and EVANS, F. A.: The energy exchange in obesity. *J. Clin. Investigation* 6:277, 1928.

4a. EVANS, F. A., and STRANG, J. M.: The treatment of obesity with low caloric diets. *J.A.M.A.* 97: 1063, 1931.

5. MILROY, A. H.: Protein metabolism in starvation in *Metabolism and Practical Medicine* (VON NOORDEN, C.), Vol. 2, W. T. Keener, Chicago, 1907, p. 1.

6. BENEDICT, F. G., MILES, W. H., ROTH, P., and SMITH, H. M.: Human vitality and efficiency under prolonged restricted diet, Publ. 280, Carnegie Inst., Pittsburgh, 1919.

7. KEYS, A., BROZEK, J., HENSHEL, A., MICKELSON, O., and TAYLOR, H. L.: *The Biology of Human Starvation*, Univ. of Minnesota Press, Minneapolis, 1950.

8. CHAIKOFF, I. L., and CONNOR, C. L.: Production of cirrhosis of the liver of the normal dog by high fat diets. *Proc. Soc. Exp. Biol. & Med.* 43:638, 1940.

9. GYÖRGY, P., and GOLDBLATT, H.: Experimental production of dietary liver injury (necrosis, cirrhosis) in rats. *Proc. Soc. Exp. Biol. & Med.* 46:492, 1941.

10. BEST, C. H., HARTROFT, W. S., and SELLERS, E. A.: The protection of the liver by dietary factors. *Gastroenterology* 20:375, 1952.

11. BEST, C. H., HARTROFT, W. S., LUCAS, C. C., and RIDOUT, J. R.: Effects of dietary protein, lipotropic factors and re-alimentation of total hepatic lipids and their distribution. *Brit. Med. J.* 1: 4928, 1955.

12. BROCK, J. F.: Chronic protein malnutrition. *Nutrition Rev.* 13:1, 1955.

13. SHERLOCK, S.: Effect of undernutrition in man on hepatic structure and function. *Nature* 161:604, 1948.

14. HELWIG-LARSEN, P., HOFFMEYER, H., KIELER, J., THAYSEN, E. H., THAYSEN, J. H., TYHGESEN, P., and WULFF, M. H.: *Famine Disease in German Concentration Camps. Complications and Sequels.* E. Munksgaard, Copenhagen, 1952.

15. SELWYN-CLARKE, P. S.: Meeting of the Nutrition Society. Discussion of nutritional experiences in prisoner-of-war and internment camps in the Far East. *Lancet* 1:852, 1946.

16. Nutrition surveys of prisoners of war. *Nutrition Rev.* 5:37, 1947.

17. MCCANCE, R. A., and WIDDOWSON, B. M.: *The Chemical Composition of Foods.* H. M. Stationery Office, London, 1956, p. 44.

18. VON NOORDEN, C.: *Metabolism and Practical Medicine*, Vol. 2, W. T. Keener, Chicago, 1907, p. 69.

19. GRAFE, E.: *Metabolic Diseases and their Treatment*, Lea and Febiger, Philadelphia, 1933, p. 70.

20. PASSMORE, R., MEIKLEJOHN, A. P., BEWAR, A. D., and THAW, R. K.: An analysis of the gain in weight of overfed thin young men. *Brit. J. Nutrition* 9:27, 1955.

21. KEYS, A., ANDERSON, J. T., and BROZEK, J.: Weight gain from simple overeating. *Metabolism* 4:427, 1955.

22. MORRISON, F. B.: *Feeds and Feeding.* Morrison, Ithaca, New York, 1954, p. 201.

23. NEWBURGH, L. H.: The cause of obesity. *J. A.M.A.* 97:1659, 1931.

23a. NEWBURGH, L. H.: Obesity. I. Energy metabolism. *Physiol. Rev.* 24:18, 1944.

24. KEYS, A., and BROZEK, J.: Body fat in adult man. *Physiol. Rev.* 33:245, 1953.

25. BATES, M. W., HAUSS, S. F., HAGMAN, N. C., and MAYER, J.: Fat metabolism in three forms of experimental obesity. Body composition. *Am. J. Physiol.* 180:301, 1955.

26. BRECHER, G., and WAXLER, S. H.: Obesity in albino mice due to single injections of gold thioglucose. *Proc. Soc. Exp. Biol. & Med.* 70:498, 1949.

27. WAXLER, S. H., and ENGER, M.: Organ weights and obesity in mice. *J. Nutrition* 54:209, 1954.

28. ZELMAN, S.: The liver in obesity. *Arch. Int. Med.* 90:141, 1952.

29. DUBLIN, L. I., and MARKS, H. H: Mortality among insured overweights in recent years. *Assn. Life Ins. Med. Dir. Am.* 35:235, 1951.

30. ALONZO, L. G., and MAREN, T. H.: Effect of food restriction on body composition of hereditary obese mice. *Am. J. Physiol.* 183:284, 1955.

31. VAN PUTTEN, L. M., VAN BEKKUM, D. W., and QUERIDO, A.: Influence of hypothalamic lesions producing hyperphagia, and of feeding regimens on carcass composition. *Metabolism* 4:68, 1955.

32. VON NOORDEN, C.: Citation of VON NOORDEN C. and DAPPER, C. 1893, in *Metabolism and Practical Medicine*, Vol. 2, W. T. Keener, Chicago, 1907.

33. KEETON, R. W., and DICKSON, D.: Excretion of nitrogen by obese patients on diets low in calories, containing varying amounts of protein. *Arch. Int. Med.* 51:890, 1933.

34. BENEDICT, F. G.: *A Study of Prolonged Fasting.* Publ. 203, Carnegie Inst. Pittsburgh, 1915.

35. STIEBELING, H. K., and SHIPARD, E. F: Diets of families of employed wage earners and clerical workers in cities. *Circ.* 507, U. S. Dept. Agr., Wash., D. C., 1939.

36. Food Balance Sheets. Food and Agriculture Org. U. N., 2nd issue, Rome, 1955.

37. Nutritive value of diets of urban families, United States, Spring 1948 and comparison with diets in 1942. 1948 Food Consumption Surveys. Prelim. Rept. 12, U. S. Dept. Agr., Wash., D. C., 1949.

38. DOLE, V. P.: A relation between dietary protein and total calorie intake of large population groups. AM. J. CLIN. NUTRITION 5:72, 1957.

39. FRYER, J. H., MOORE, N. S., WILLIAMS, H. H., and YOUNG, C. M.: A study of the interrelationships of the energy-yielding nutrients, blood glucose

levels, and subjective appetite in man. *J. Lab. & Clin. Med.* 45: 684, 1955.

40. STRANG, J. M., MCCLUGAGE, H. B., and EVANS, F. A.: Further studies in the dietary correction of obesity. *Am. J. Med. Sc.* 179: 687, 1930.
41. EVANS, F. A.: *Diseases of Metabolism* (C. G DUNCAN), W. B. Saunders Co., Philadelphia, 1952, p. 648.
42. RONY, H. R.: *Obesity and Leanness.* Lea & Febiger, Philadelphia, 1940, p. 246.
43. MASON, E. H.: The treatment of obesity. *Can. M. A. J.* 14: 1052, 1924.
44. DOLE, V. P., SCHWARTZ, I. L., THAYSEN, J. H., THORN, N. A., and SILVER, L.: Treatment of obesity with a low protein calorically unrestricted diet. AM. J. CLIN. NUTRITION 2: 381, 1954.
45. AHRENS, E. H., JR., DOLE, V. P., AND BLANKENHORN, D. H.: The use of orally-fed liquid formulas in metabolic studies. AM. J. CLIN. NUTRITION 2: 336, 1954.
46. KEETON, R. W., and BONE, D. D.: Diets low in calories containing various amounts of protein. *Arch. Int. Med.* 55: 262, 1935.
47. KEKWICK, A., and PAWAN, G. L. S.: Caloric intake in relation to body weight changes in the obese. *Lancet* 2: 155, 1956.
48. BOOTH, G., and STRANG, J. M.: Changes in temperature of the skin following ingestion of food. *Arch. Int. Med.* 57: 533, 1936.
49. KESTNER, O.: 1919: cited by DARBY, W. J. in MCLESTER, J. S., and DARBY, W. J.: *Nutrition and Diet in Health and Disease,* ed. 6, W. B. Saunders Co., Philadelphia, 1952, p. 130.
50. MAYER, J.: The physiological basis of obesity and leanness. *Nutrition Abs. & Rev.* 25: 597, 1955.
51. GLOMSET, D. A.: The role of the physician in weight control, *Weight Control Colloquium.* Iowa State Coll. Press, Ames, 1955, p. 211.
52. MAYER, J.: The role of exercise and activity in weight control, *Weight Control Colloquium* Iowa State Coll. Press, Ames, 1955, p. 199.